WO 99/25727

01/09

#### EXENDIN-3

His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu

1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser

20 25 30

Ser Gly Ala Pro Pro Pro Ser-NH<sub>2</sub>

## Fig. 1

#### EXENDIN-4

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser 20 25 30

Ser Gly Ala Pro Pro Pro Ser-NH, 35

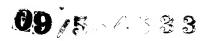
## Fig. 2

#### $GLP-1 (GLP-1[7-36]NH_2)$

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg-NH<sub>2</sub>
20 25 30

## Fig. 3



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2	Ser Lys Gin Met Glu Glu Glu Ata Val Arg Leu Phe	Ser Lys Gin Leu Glu Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Met Glu Glu Glu Ala Val Arg Leu	Ser Lys Gin Leu Giu Giu Ala Val Arg Leu	Lys Gin Leu Glu Glu Glu Ala Val Arg Leu	<u>E</u>	Thr Ser Asplea Ser Lys Gin Leu Glu Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Mei Glu Glu Glu Ala Val Arg Leu Phe	ច	5	Ser Lys Gin Met Glu Glu Glu Ala Val Arg Leu Phe	HS US	뜅	Ser Lys Gin Met Glu Giu Glu Ala Val Arg Leu	Ser Lys Gin Met Giu Giu Giu Ala Val Arg Leu Phe	땅	Ser Lys Gin Met Glu Glu Glu Ala Val Arg Leu	Ser Lys Gin Met Glu Glu Glu Ala Val Arg Leu	Ser Lys Gin Met Ala Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Leu Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Leu Giu Giu Giu Ala Val Arg Leu naph lle	Ser Lys Gin Mei Glu Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Leu Glu Glu Glu Ala Val Arg Leu Phe	Ser Lys Gin Leu Giu Giu Giu Ala Val Arg Leu Phe	Ser Lys Gin Met Glu Glu Glu Ata Val Arg Leu Phe	Ser Lys Gin Mei Giu Giu Giu Aia Val Arg Leu Phe
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10 11					in Ser I	S	S n	S D	n Ser							u Serll		_		sly Se				_		
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8	SerA	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Ser	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	SerlA	Ser Ser Asp Leu	Ser Thr Asp Leu	Ser GI	Thr Ser Asp pGly	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Leu	Thr Ser Asp Ala	Thr Ser Asp Ala	Thr Ser Asp Ala
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7	GlyG	S S	Gy G	Gly G	Gly G	G G	Gly G	Gly G	Gly G	Gly G	Sly G	Gly G	Gy G	Gly G	Sy. A	Sly G	3ly lG	3k	Sly G	<u>ල</u>	Gly Glu Gly Thr Phe	3 <del>)</del> (3	<u>응</u>	읭	읡	읡
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Amino Acid Position	Compound 36 His Gly Glu Gly Thr Phe	Compound 37 His Gly Glu Gly Thr Phe	Compound 38 His Gly Glu Gly Thr Phe	Compound 39 His Gly Glu Gly Thr Phe	Compound 40 His Gly Glu Gly Thr Phe	Compound 41 His Gly Glu Gly Thr Phe	Compound 42 His Gly Glu Gly Thr Phe	Compound 43 His Gly Glu Gly Thr Phe	Compound 44 His Gly Glu Gly Thr Phe	Compound 45 His Gly Glu Gly Thr Phe	Compound 46 His Gly Glu Gly Thr Phe	Compound 47 His Gly Glu Gly Thr Phe	Compound 48 His Gly Glu Gly Thr Phe	Compound 49 Arg Gly Gly Gly Thr Phe	Compound 50 His Gly Asp Gly Thr Phe	Compound 51 His Gly Glu Gly Thr naph Thr Ser Asp Leu	Compound 52 His Gly Glu Gly Thr Phe	Compound 53 His Gly Glu Gly Thr Phe	Compound 54 His Gly Glu Gly Thr Phe	Compound 55 His Gly Glu Gly Thr Phe	Compound 56 His	Compound 57 His Gly Glu Gly Thr Phe	Compound 58 His Gly Glu Gly Thr Phe	Compound 59 His Gly Glu Gly Thr Phe	Compound 60 His Gly Glu Gly Thr Phe	Compound 61 His Gly Glu Gly Thr Phe
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PCT/US98/24210

04/09

# Glucose lowering effect in db/db mice at 1 hr time point

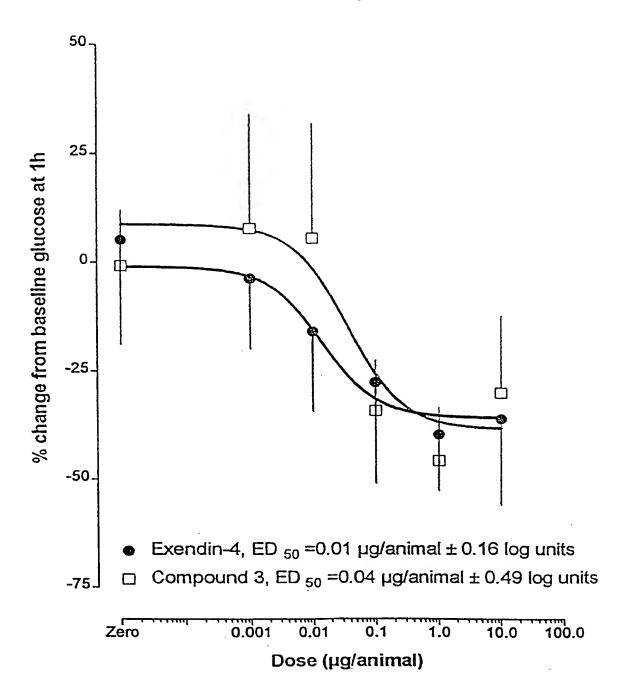
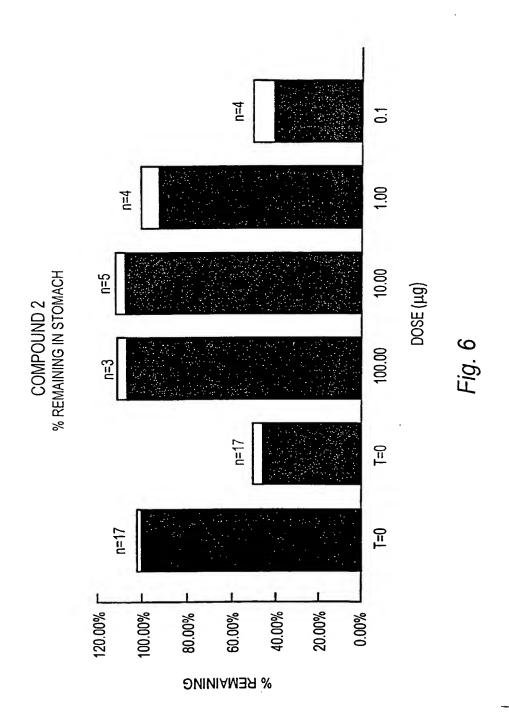
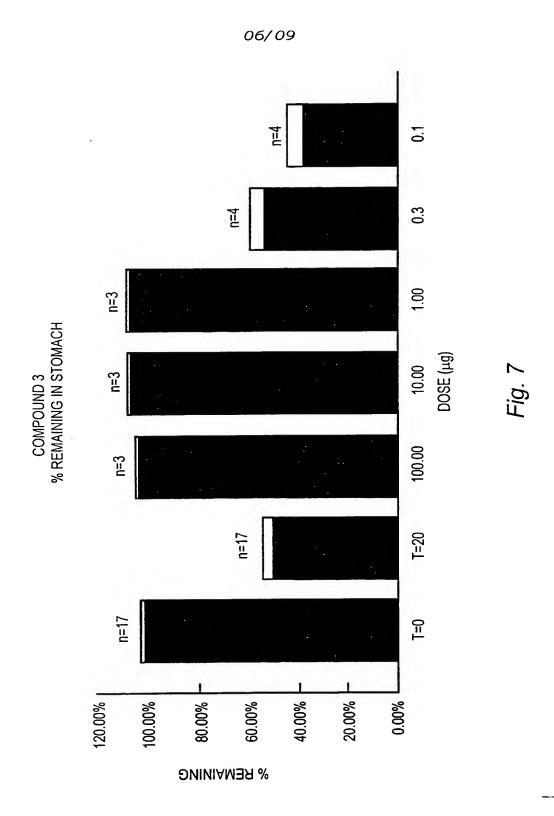


Fig. 5
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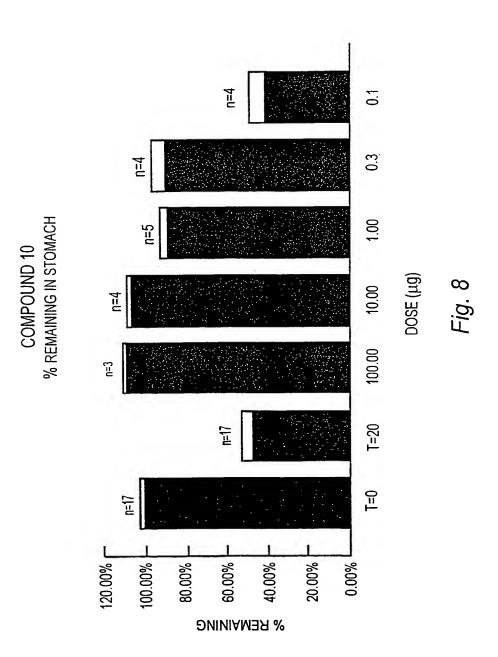


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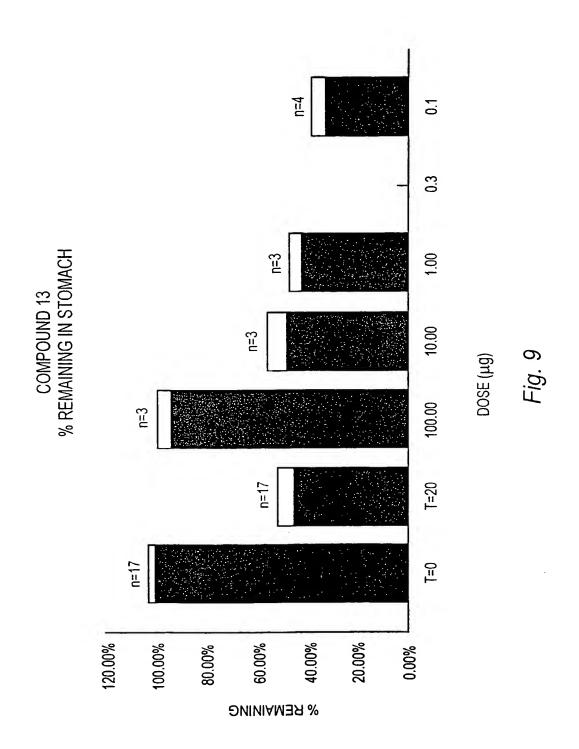


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Compound

09/55	45	3	3
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09/09 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val ID NO. 70] 73] 69] 74] [SEQ. [SEQ. ID NO. ID NO. ID NO. 71] 72] 67] Arg Leu Phe Ile Glu Phe Leu Lys-NH'octanoyl Asn Gly Gly-NH, [SEQ. [SEQ. (SEQ. ID NO. [SEQ. ID NO. ID NO. ID NO. Phe Ile Glu Trp Leu Lys-NH'octanoyl Asn Gly Gly-NH2 Phe Ile Glu Phe Leu Asn Lys-NH'octanoyl Gly Gly-NH, Phe Ile Glu Trp Leu Asn Lys-NH'octanoyl Gly Gly-NH, (SEQ. (SEQ. Phe Ile Glu Trp Leu Lys-NH'octanoyl Asn-NH, Phe Ile Glu Phe Leu Lys-NHtoctanoyl Asn-NH, Phe Ile Glu Trp Leu Asn Lys-NHtoctanoyl-NH, Phe Ile Glu Phe Leu Asn Lys-NH'octanoyl-NH, 65 99 67 69 62 63 64 68